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Experience of West Nile Virus Testing

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An arbovirus known to cause encephalitis primarily in animals was first isolated in the United States from a dead crow on September 14, 1999. It was identified to be West Nile Virus (WNV), originally discovered in the West Nile District of Uganda. After first demonstration in New York, it spread to Connecticut, New Jersey and Maryland in 2000. The Michigan Department of Community Health (MDCH) was awarded a grant in June 2000 from Centers for Disease Control and Prevention (CDC) to conduct WNV surveillance. In a cooperative plan with the Michigan Department of Agriculture (MDA), Michigan Department of Natural Resources (MDNR) and Michigan State University's Animal Health Diagnostic Laboratory (AHDL) and Department of Entomology, surveillance focused on the collection and testing of dead crows and blue jays from May through September of 2001. The surveillance resulted in identifying positive birds, as well mosquito pools, in Michigan. One hundred fifty-nine human specimens were also tested in a serologic panel for the arboviruses, including WNV, St. Louis encephalitis (SLE), Eastern equine encephalitis (EEE) and California group virus encephalitis (CGV). None was found positive for WNV.

The surveillance guidelines were revised for the year 2002, with the addition of a hot line and a web site for citizen reporting of dead bird sightings. Reports to the hot line in 2002 totaled more than 35,000 calls. Seventy-three out of 83 participating counties in the state submitted birds which tested positive for WNV.

The first line test utilized for diagnosis of WNV is IgM-capture enzyme-linked immunosorbent assay (MAC-ELISA). This test is used for the serological diagnosis of WNV from serum as well as cerebrospinal fluid (CSF), the later being the preferred sample for diagnosis. A positive IgM on CSF is sufficient to establish a diagnosis of WNV. Other tests employed are IgG ELISA and Plaque Reduction Neutralization Test (PRNT). A fourfold rise in IgG titers in paired sera drawn in acute and convalescent stages (at least 21 days apart) can distinguish a recently acquired infection from a past infection. To rule out the cross-reactions between WNV and other arbovirus infections (SLE, EEE and CGV), specificity of the antibody in the specimen is confirmed by PRNT.

Requests to MDCH for arboviral testing began at the end of April 2002, due to heightened awareness on the part of physicians. The first confirmed case of WNV was in the week of August 11, with the volume of requests increasing dramatically thereafter. Due to limited resources, guidelines for expedited testing specimens were developed. A patient ill enough to have a spinal tap for diagnosis of meningitis, encephalitis or meningo-encephalitis was given the priority over those who had just fever, who did not need hospitalization or on whom only a serum sample was submitted. Using the CDC case definition and guidelines, algorithms for testing were refined. Communication of positive results was expedited by using an electronic system of reporting results to local health departments, submitter and the MDCH epidemiology program.

From January 1, 2002 until December 21, 2002, the virology section received a total of 2,890 human specimens for arboviral testing. A weekly analysis of the submissions and the confirmed positive cases is shown in Fig. 1.

MDCH was involved in the investigation of the transmission of the WNV through blood products, organ transplants and breast milk (MMWR-2002; 51 (39):877-879. It was through the efforts of dedicated staff who worked overtime during this WNV season that MDCH was

able to accomplish testing in the shortest possible time. The authors acknowledge this contribution, with thanks to all the sections that extended help in this endeavor.

Due to the continued concern for acquisition of WNV infection by travelers to the south and transmission via blood transfusion, MDCH will continue testing for the arboviruses during the winter months, unlike previous years when testing was performed only from May through October. Serological data collected this year will be analyzed to determine future testing protocols.

There is much not known about the behavior of this virus in North America, specifically in the MidWest, including its effect upon bird populations and how the role of different species of mosquitos play in transmission. There is one fact which is certain; WNV is in Michigan.

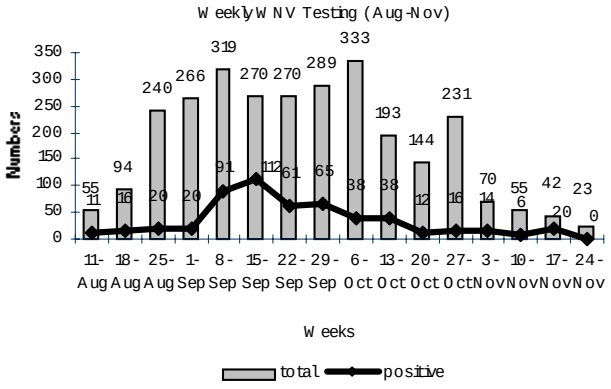

Figure 1

Newborn Screening Information System Update

Harry C. Hawkins, B.S.

Division of Chemistry and Toxicology
Newborn Screening Unit

After much planning and talking, the new information system in the newborn screening laboratory is becoming a reality. Plans have been made for the testing and implementation of the software. There are many components that must be validated before putting them all together to test complete modules in the system. At the time of this writing, the new network server has been installed and some of the new software has been tested.

There will be some significant changes for submitters sending samples to the laboratory. The most obvious is the new specimen collection card for the heel stick sample. A larger card will enable scanning demographic information into the system. One new feature is a separate copy slip of the demographic information to be kept by the submitter for their records. There will still be a hearing screening result sheet to be torn out, checked off, and mailed separately. The hearing results will be scanned directly into a database without key entry.

Other changes to the information card include fields for date and time of birth and specimen collection so the baby's age in hours will not have to be calculated by the submitter. There is space for the person collecting the sample to write their initials. An overlay flap will protect the filter paper before specimen collection. The circles are a bit farther apart and this may help to prevent the blood circles from running together.

The pre-addressed envelopes provided by the program for submitting samples will be larger and no longer yellow in color. The envelope bar code will enable faster, accurate delivery by the postal service. There will be a firm date on which the switch to the new cards will occur. This date will depend on many factors and is subject to change. The target date is March 3, 2002. Submitters are asked to order specimen cards in numbers sufficient for month-to-month operation so that swapping out large quantities can be avoided.

Another change is the use of secure fax machines to receive results faxed out automatically. Consistent with other result faxing procedures within the Bureau of Laboratories, submitters can choose to receive their newborn screening results directly to a facsimile machine that has been declared to be "secure." A secure fax machine must be operational 24 hours, seven days a week, be restricted to only persons authorized to review confidential laboratory results and must also be in a secure location during non-business hours. Results will be reported out several times a day and those that are not faxed will be printed and mailed through the U.S. Postal Service. There will be a noticeable decrease in turnaround time for negative results because the result boxes that are currently checked off will be eliminated. One change from the previously cited *LabLink* article is that the option to receive results via email will not be available immediately. Please contact newborn screening at (517) 335-9205 with any questions regarding the new database.

Clinical Microbiologists Play Key Role in Michigan Smallpox Vaccination Plan

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On December 13, 2002, President Bush announced the plans for a national smallpox vaccination effort. This public announcement came after weeks of dedicated effort of MDCH staff from the Bureau of Laboratories (BOL), Bureau of Epidemiology, and the recently established Office of Public Health Preparedness to prepare a state pre-event smallpox plan.

Smallpox planning is a part of Michigan's homeland security efforts. The pre-event smallpox vaccination plan for Michigan, written with guidance from CDC and other scientific agencies as well as input from local health partners throughout the state, was submitted to CDC in early December, 2002. The plan will provide the smallpox vaccine, a suspension of live vaccinia virus, to the population of Michigan in stages, through the use of teams established by state and local health departments and hospitals.

Two State Public Health Response Teams (SPHRT) are responsible for coordination with and vaccination of Public Health Response Team members (PHRT), which have been established in each of the eight emergency response regions in the state (see Figure 1). The PHRT in turn will coordinate with and vaccinate the Health Care Response Teams (HCRT) identified in designated hospitals in each of these eight regions. These regions were based upon the Michigan State Police Emergency Management Response regions and do not respect the boundaries of some district health departments or correspond to the Michigan Bioterrorism Laboratory Response System. The MDCH pre-event smallpox vaccination plan is a voluntary vaccination plan and is designed in three phases.

Phase I will vaccinate approximately 5,000-7,000 individuals identified as members of the teams (SPHRT, PHRT and HCRT) within 30 days of initiating the plan. These professionals would play a key role in the initial response to a smallpox bioterrorism event. This includes a limited number of hospital personnel to care for smallpox patients, teams of vaccinators who could quickly vaccinate a large number of people against smallpox and public health personnel to investigate and respond to the outbreak. Designated MDCH lab testing personnel involved in vaccinia testing are included in this group. Clinical and hospital-based laboratorians are not included in this phase as the handling of specimens from suspect patients, once collected, is deemed to be low risk. However, those who would be expected to provide phlebotomy services for suspect cases should be vaccinated at this stage.

Phase II of the plan is an expansion of Phase I and will follow soon after the completion of Phase I. It will include additional health care workers, emergency responders, police and fire fighters and will probably include several thousand individuals. Clinical laboratorians will most likely be included in this phase. It is expected that this phase will be completed within 45-90 days once it is begun.

Phase III of the smallpox plan, should it be implemented, involves vaccination of the general public.

Public opinion in favor of general vaccine availability has declined as information about the risks of the vaccine is made available. Because it is a live virus vaccine, the response to vaccination involves development of a local acute infection which conveys immunity. Those with impaired immunity, especially of a type which would affect cellular immunity, such as infection with HIV, transplant and chemotherapy recipients, may fail to contain the infection to the inoculation site and may experience a generalized, at times life-threatening infection. Likewise, those with certain skin conditions such as eczema may suffer a generalized infection. Those who are pregnant and children are also excluded from pre-event receipt of this vaccine. Also, anyone living with a person with any contraindications should not be vaccinated in the pre-event phase. For more complete information related to smallpox, smallpox vaccine, adverse reactions to or contraindications of the vaccine, please see the MDCH website at http://www.michigan.gov/mdch (click on "Smallpox information"). In the unlikely event that smallpox itself is reintroduced, there are no contraindications to vaccine for someone who has been exposed.

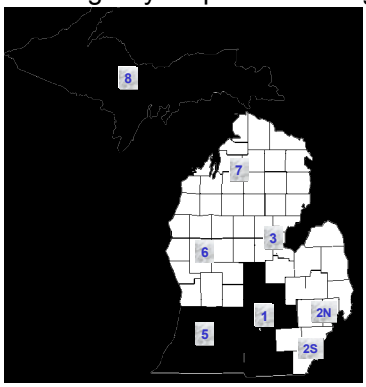
The MDCH laboratory is currently capable of testing for VZV, vaccinia, HSV, and enteroviruses, the etiologic agents of rash-like illnesses most likely to be confused with smallpox (variola) and anticipate designation by CDC as one of the LRN laboratories with variola-specific testing capability. Guidelines for collection and transport of specimens from these vesicular/pustular rash-type illnesses have been distributed to local health departments, as well as the laboratory and emergency department of each hospital. Those hospitals participating in Phase I have, in addition, received collection kits (Unit #20). Eventually all hospitals will receive these collection kits upon request. Each laboratory should have received a copy of specimen collection guidelines. Contact Valerie Reed, Laboratory Bioterrorism Preparedness Coordinator at 517-335-9653 or ReedV@michigan.gov if this is not the case.

Clinical microbiologists will play an essential role in the smallpox preparedness plan. With the reintroduction of the smallpox vaccine, an increase of cases of vesicular/pustular rash-like illnesses presenting to emergency departments (ED) around the country is anticipated. Some of these will be vaccinees experiencing responses considered within the normal range of reaction. Others will be vaccinees experiencing severe reactions or dissemination due to an unrecognized immune impairment. A third group of individuals will be those who have no history of vaccination and those with or without knowledge of a close contact receiving the vaccine. These cases will cause a high level of anxiety among health care providers, as differentiation from smallpox, as well as herpes, varicella, enterovirus, will have to be made. Clinical

microbiologists in Michigan will be a ready source of guidance and support for ED staff. Through such clinical laboratory involvement, appropriate testing to demonstrate the cause of these rash-like illnesses can be provided. MDCH is confident in the support provided to the medical community by our clinical microbiology partners as the first vaccine program in over 30 years is undertaken.

Figure 1. MI Public Health Preparedness Regions

Emergency Preparedness Regions



Preventing Antimicrobial Resistance in Hospitalized Patients

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In March 2002, the CDC launched the first of eight planned 12-step intervention programs to prevent antimicrobial resistance in healthcare settings. This first program, "12 Steps to Prevent Antimicrobial Resistance in Hospitalized Adults", translates science-based evidence and published guidelines into practical action steps that can be taken by physicians.

At first glance, this clinician-focused program may seem inapplicable for the laboratory, but a closer look reveals good reasons for microbiologists and other patient care partners to become familiar with it. Raising awareness about increasing antimicrobial resistance, its prevalence and consequences, including the costs of inappropriate antimicrobial use, will benefit patients and can help the microbiology laboratory manage its ever-increasing daily workload.

There are four key strategies in the program:

1. Prevent infection
2. Diagnose and treat infection effectively
3. Use antimicrobials wisely
4. Prevent transmission

These strategies are divided into 12 practical actions that clinicians can take to manage infectious disease; and which, if used in daily practice, will prevent the emergence and spread of resistance:

1. Vaccinate
2. Get the catheters out
3. Target the pathogen
4. Access the experts
5. Practice antimicrobial control
6. Use local data
7. Treat infection, not contamination
8. Treat infection, not colonization
9. Know when to say "no" to vanco
10. Stop treatment when infection is cured or unlikely
11. Isolate the pathogen
12. Contain the contagion

Because the microbiology laboratory is directly involved with at least seven (#3-9) of the 12 steps, it is very important to know what is being presented to the clinicians. The background, prevalence and trends of resistance are discussed succinctly. The recommendations with regard to cumulative antibiograms, infectious disease consultation, oversight of antibiotic prescribing and positive blood culture interpretation will benefit patients. Finally, the discussion of contamination or colonization versus true infection will give powerful support when dealing with inappropriate requests for susceptibility testing.

What can the laboratory do? Become familiar with the campaign. MDCH has a copy on CD which is available through our training library. Contact Susan Shiflett at 517-335-9972 or shifletts@michigan.gov to arrange to borrow a copy. Copies may also be obtained in either adobe (pdf) or Power Point format (2.3MB) directly from CDC at http://www.cdc.gov/drugresistance/healthcare/patients.htm. Those laboratories with training programs should consider the using the CD as a tutorial for medical students and residents during their microbiology or infectious disease rotation. Promote the principles of the campaign among practicing physicians, pharmacists, infection control practitioners, infectious disease specialists and the medical education department within your institution. Contact Marty Boehme at 517-335-9654 or boehmem@michigan.gov for more information on this or other antimicrobial resistance topics.

What's in a Name?

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Accurate identification of *Salmonella* requires both biochemical identification and serotyping. Serotyping has become the foundation of epidemiologic surveillance and outbreak investigations. Over the years, the nomenclature of the *Salmonella* species has changed several times. In recent years, the Centers for Disease Control and Prevention (CDC) has used the "Modified Kauffman-White Scheme" for *Salmonella*. The World Health Organization (WHO) and most other countries use the Kauffmann-White Scheme. Beginning in January 2003, CDC will adopt the Kauffmann-White Scheme for *Salmonella* serotype designation to improve the accuracy of surveillance data and to make data from the United States comparable with the rest of the world. MDCH will begin a transition to the new scheme in early 2003.

In both typing schemes, the genus Salmonella is divided into two species, *Salmonella enterica* and *Salmonella bongori*. *Salmonella enterica* is further subdivided into six subspecies that are designated by names or Roman numerals: *S. enterica* subsp. *enterica* (I), *S. enterica* subsp. *salamae* (II), *S. enterica* subsp. *arizonae* (IIIa), *S. enterica* subsp. *diarizonae* (IIIb), *S. enterica* subsp. *houtenae* (IV), and *S. enterica* subsp. *indica* (VI). *S. bongori* was originally designated *S. enterica* subspecies V, but is now considered to be a separate species. Most of the 2,435 *Salmonella* serotypes that are usually isolated from humans belong to subspecies I. Under the Kauffmann-White Scheme, subspecies I serotypes are named (e.g., *Salmonella* Typhimurium), while subspecies II through VI serotypes are identified by antigenic formula.

The antigenic formula is based on the presence of two surface structures, O antigen and H antigen. The somatic polysaccharide or O antigens are divided into groups usually designated by letter (A, B, C, D, etc.). Each O group possesses at least one unique antigen that is usually designated by number. For example, all group B organisms possess antigen 4 and all group E_1 organisms possess antigens 6 and 14. Salmonella may express two different H or flagella antigens in motile strains. Typically only one antigen is expressed at a time in a single bacterial cell. The two antigens are referred to as Phase 1 and Phase 2. Lowercase letters, numbers, or a combination of both designate H antigens. The format for the antigenic formula is: Subspecies O antigens: Phase 1 antigen: Phase 2 antigen. So the antigenic formula for *S.* Typhimurium would be I 4,5,12:i:1,2.

Currently, CDC uses names for those subspecies II through VI serotypes that were named before 1968 and uses formulas for serotypes identified after 1968. Under the new scheme subspecies I serotypes will be named only; all other subspecies will be identified by formula. This means that several organisms MDCH currently reports by name will now be reported by formula. For example, *S.* Flint will now be designated as *S.* IV 50:z_4,z_{23}:-. In order to minimize the confusion associated with this change, MDCH will report serotypes according to the Kauffmann-White scheme, but will continue to report the serotype name in parenthesis; *S.* Flint will be reported as *S.* IV 50:z_4,z_{23}:- (formerly Flint).

Serogroups E_2 and E_3 are combined with serogroup E_1 using the Kauffmann-White Scheme. This reflects the fact that the antigenic changes in serogroup E_2 and E_3 are the result of lysogenic conversion by bacteriophages and thus represent minor variants of serogroup E_1. Two serotypes in the top 100 will be affected by this merging of serogroup. *S*. Newington will become *S*. Anatum variety (var.) 15+; and *S*. Newbrunswick will become *S*. Give var. 15+.

The third difference between the current reporting scheme and Kauffmann-White concerns *S*. Java. *S*. Paratyphi B and *S*. Java has the same antigenic formula (I 1,4,[5],12:b:1,2), but can be differentiated by tartrate fermentation; *S*. Paratyphi B is tartrate negative and *S*. Java is tartrate positive. The distinction between these serotypes is important clinically because *S*. Paratyphi B is associated with a more severe typhoid-like disease. Using the Kauffmann-White Scheme both isolates would be reported as *S*. Paratyphi B, but *S*. Java will now be reported as *S*. Paratyphi B var. tartrate +.

This transition in *Salmonella* reporting will probably result in some confusion for both laboratorians and clinicians. MDCH will continue to report the old serotype name designation in parenthesis after the new designation. CDC has also established a website that will present the new and old schemes as well as allow you to search for serotype designation based on any part of the antigenic formula, the old name or the new name.

The website can be found at http://www.cdc.gov/ncidod/dbmd/foodborne/index.htm. Questions regarding the changes in nomenclature at MDCH may be addressed to Carrie Anglewicz at (517) 335-8133 or AnglewiczC@michigan.gov.

Newborn Screening Laboratory Will Add MCAD Deficiency Testing

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Newborn Screening Unit

These are busy times in the newborn screening laboratory. The laboratory tests dried filter paper blood samples from all babies born in Michigan for metabolic conditions that can cause death or developmental disabilities if not promptly treated. In addition to the implementation of the new information system described earlier in this *LabLink* issue, MDCH will add another disorder to the list of seven already screened.

The new test will be for medium-chain acyl-coenzyme A dehyrogenase deficiency, more easily referred to as MCAD deficiency, or MCADD. This is a rare inborn error of metabolism in which certain fats cannot be broken down and metabolized into energy. It is expected to have an incidence rate more frequent than that of phenylketonuria (PKU). MCAD is one of four enzymes in the mitochondria responsible for the breakdown of medium-chain (C4-C14) fatty acids to 2-carbon fragments (acetyl-CoA) in the beta oxidation pathway. This is the most common fatty acid oxidation defect. There are 3 straight-chain acyl-CoA dehydrogenases to deal with long, medium and short chain fatty acids.

During times of stress (e.g., illness, fasting, fever, etc.), when the metabolic rate is high and/or energy stores from food are low, the body is not able to convert fats into sugar. Babies with this disorder can become extremely hypoglycemic and even die. A baby may remain asymptomatic and appear healthy for long periods of time but then present suddenly and fatally as a Sudden Infant Death Syndrome-like (SIDS). Usually, it affects children older than the typical SIDS age. Newborn screening can identify an infant with MCAD deficiency and parents can be educated to avoid fasting conditions and to seek immediate help if symptoms occur. Up to 25 percent of MCAD patients do not survive their first acute episode. It is predicted that this testing program will identify approximately 20 babies annually who are at risk for MCAD.

Testing for MCADD has become possible due to relatively recent developments in an old technology. Mass spectrometry has been in laboratories for more than 30 years and in newborn screening for almost 10 years. This expensive instrument has been modified for the dried spot heel stick sample. Computerization has brought down the cost for screening high volumes of specimens in the laboratory. The laboratory will use tandem mass spectrometry (TMS), two mass spectrometers linked together. This instrument can be used to identify the defective breakdown of fatty acids and branch-chain amino acids by detecting the presence of abnormally high levels of particular carnitines in the same sample.

H.B. 5998 mandates MCAD screening to start on April 1, 2003. MDCH laboratory staff are busy validating a new TMS instrument and developing normal ranges and cutoffs for MCAD. Another instrument must be installed to handle the annual volume of 140,000 samples per year.

Newborn screening is a comprehensive program to ensure that babies identified through laboratory tests get proper follow-up. Efforts are now being made to line up the resources needed to provide appropriate diagnostic evaluation and treatment for the MCAD patients who will be identified. With the addition of this technology, a new test and a new database, this is the busiest time in the newborn screening laboratory since hemoglobinopathies, biotinidase deficiency and maple syrup urine disease (MSUD) were added to the test battery in 1987. Please contact newborn screening at (517) 335-9205 with any questions regarding the implementation of MCAD screening.

E. coli Toxin Testing Change

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Enteric/STD/Chromatography Unit

The microbiology laboratory has been examining *Escherichia coli* cultures for the ability to produce Shiga-like toxins one and two (Stx1 and Stx2) since 1997 by an in-house developed DNA probe assay. These toxin producing organisms are strongly implicated with hemorrhagic colitis and hemolytic uremic syndrome (HUS), particularly in children. This manifestation may result in kidney failure and even death.

During November 2002, the MDCH microbiology laboratory upgraded this service from a DNA probe to a polymerase chain reaction (PCR) assay. This change will increase sensitivity and provide the ability to detect mutations in the toxin genes by detecting melting temperature changes in the target DNA.

All *E. coli* cultures submitted for serotyping are examined by PCR for the ability to produce Stx1 and/or Stx2. Those strains positive for either toxin are serotyped. Any isolates that are unable to be typed at MDCH, due to the limited number of antisera available, are sent to CDC for complete serotyping. Cultures negative for Stx1 and Stx2 are reported "serotype unknown." *E. coli* culture reports will appear the same as they were with DNA probe results.

The following table shows the results of *E. coli* serotyping and toxin testing performed at MDCH since 1997. Note that a majority of O157 cultures produce Stx toxins but some do not. Several other serotypes have the ability to produce Stx toxins but they are detected less frequently than O157 strains. Some O157 and most non-O157 cultures are able to utilize sorbitol making them more difficult to distinguish from typical *E. coli* using O157 screening procedures. (See table page 5)

Serotype	Stx1 and Stx 2 Pos.	Stx 1 Pos./ Stx 2 Neg	Stx 1 Neg/ Stx 2 Pos	Stx 1 and Stx 2 Neg.
O157:H7	481	8	118	5
O157MN	8	0	18	2
O157:H12	0	0	0	1
O157:H45	0	0	0	1
O18:H7	0	0	0	1
O22:H8	1	0	0	0
O26:H11	0	3	0	0
O45:H2	0	4	0	0
O55:H7	0	1	0	0
O91:NM	1	0	0	0
O103:H2	0	1	0	0
O110:H28	0	1	1	0
O111:NM	1	0	0	0
O119:H28	0	1	0	0
O121:H19	0	1	0	0
O145:NM	0	0	1	0
O171:H2	0	1	0	0
O Undetermined: H8	0	1	0	0
O Undetermined: H52	0	1	0	0
O Undetermined :NM	1	0	0	0
Unknown	0	0	0	1580
Total	493	22	139	1590

NM = Nonmotile

The Use Of The Quantiferon Assay In The Diagnosis Of Latent Tuberculosis

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In 2001, the Food and Drug Administration approved the *in vitro* assay, QuantiFERON-TB (QFT), as an adjunct to the diagnosis of latent infections causes by *Mycobacterium tuberculosis*. Samples of heparinized blood are used to determine a quantitative measure of interferon-gamma. Although the standard tuberculin skin test (TST) measures a component of the cellular immune system, it is not the same immune reactant that is measured by the QuantiFERON assay.

The advantages for using the QFT test over the TST include: it does not require a second visit to interpret results, it is less subject to individual interpretative error and it does not cause an anamnestic immune response.

The CDC is recommending the use of the QFT for populations that are at high risk for latent tuberculosis. These populations would include recent immigrates from high prevalence geographic areas, injection-drug users and residents and employees of penal facilities.

The CDC is not currently recommending the QFT for the diagnosis of suspected tuberculosis based on the lack of sufficient data regarding its reliability in this population. In addition, it is not being recommended for contact investigation, post PPD vaccination efficacy, diagnosis of infections caused by *M.avium* complex or for the screening of children, individuals with human immunodeficiency virus infection or pregnant women.

Outdated Collection Materials

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Enteric/STD/Chromatography Unit

The MDCH laboratory is seeing an increase in specimens submitted in outdated transport media or collected using an outdated collection device. This includes dry swabs used for *Chlamydia*/gonorrhea testing. Specimens collected using outdated media or materials cannot be tested. This will cost everyone in wasted time and money. Please regularly check specimen collection materials outdates. Discard any outdated materials and order replacements. This helps you, the lab and ultimately the patients. Replacement kits may be ordered by faxing 517-335-9039 or phoning 517-335-9867.

FUN FUNGI.....

Differentiating *Coccidioides immits* From *Malbranchea* spp.

Sandy Arduin MT(ASCP) & Bruce Palma MT(ASCP) - Mycobacteriology/Mycology Unit

Coccidioides immitis

Coccidioidomycosis is a disease caused by the fungus *Coccidioides immitis*. *C. immitis* is found in the soil of semi-arid regions and is endemic in the southwestern United states and northern Mexico. Conidia are highly infectious and are distributed by disturbances to the soil such as windstorms, farming, construction and archeological digs. Inhalation of even a few conidia can result in infection in healthy individuals. Coccidioidomycosis is a benign and transient infection of the respiratory system, which may become an acute infection disseminating to skin, bones, joints, liver, and/or central nervous system. Ninety-five percent of the those infected with *C. immitis* develop a mild infection which resolves spontaneously (i.e. without medical intervention) and results in a strong immunity against re-infection. *C. immitis* is an opportunistic pathogen in immunocompromised individuals.

Coccidioides immitis is a dimorphic fungi which forms a mould phase at 25EC and 37EC. Spherules containing endospores are formed in tissue and on special media incubated at 42EC. Rarely, it will produce hyphae forming alternating arthroconidia in cavitary lesions or air spaces in the lungs. At 25EC to 37EC growth is moderately rapid and appears glabourous to wooly. Colony growth is white, becoming brownish with age on the surface and pale to dark brown on the reverse. Atypical strains may appear gray, lavender, pink, buff, lemon yellow or brown. Microscopically, hyphae are septate and hyaline. Conidiophores are absent. Arthroconidia are unicellular, hyaline, rectangular to barrel shaped and are often somewhat wider in diameter than the hyphae. Arthrocondia alternate with empty cells (disjunctor cells). Disarticulated arthroconidia possess annular frills at both ends which are the remnants of the disjunctor cells. *C. immitis* is a dangerous mould and should only be manipulated with caution in a Class II biological safety cabinet in a BSL 2 or BSL 3 containment laboratory.

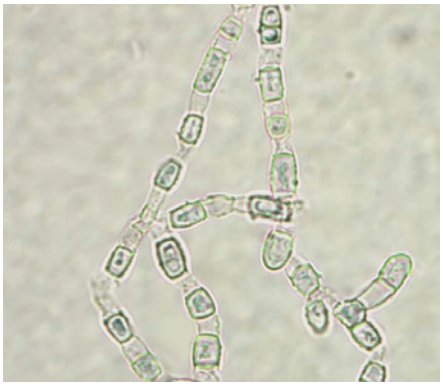
***Malbranchea* spp.**

Malbranchea spp. have been isolated from soil, animal dung, and decaying plant materials. *Malbranchea* spp. produce moderately rapid growth which appears powdery to wooly. The colony color may be white, yellow, tan, orange or greenish. Microscopically, hyphae are hyaline, septate and branched and may be straight or spirally twisted. Conidiophores are absent. Arthroconidia are unicellular, rectangular and are separated from each other by sterile empty cells (disjunctor cells). Generally, arthroconidia are of the same diameter as the hyphae from which they were formed. *Malbranchea spp.* should be manipulated in a biological safety cabinet until identification of *C. immitis* is ruled out.

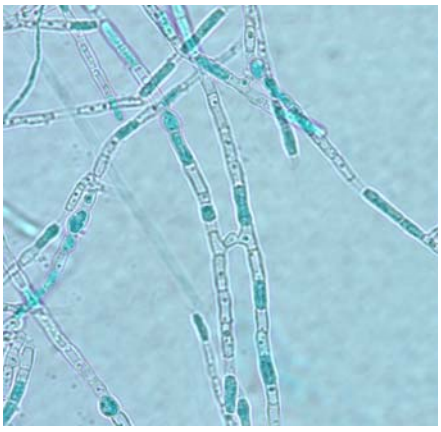
***Coccidioides immitis* vs. *Malbranchea* spp.**

Malbranchea spp. differ from *Coccidioides immitis* in several ways. *C. immitis* is a dimorphic fungi and *Malbranchea* spp. are monomorphic. *Malbranchea* spp. produce arthroconidia which are smaller and more cylindrical than the barrel shaped arthroconidia of *C. immitis*. The arthroconidia in *Malbranchea* spp. also vary in length and have irregular spacing. The two species are best differentiated by using either a specific exoantigen or nucleic acid probe test.

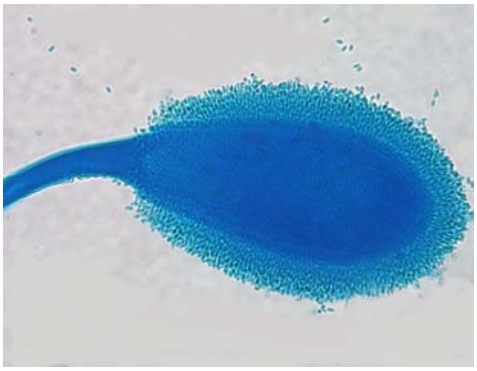
Coccidiodes immitis



***Malbranchea* spp.**

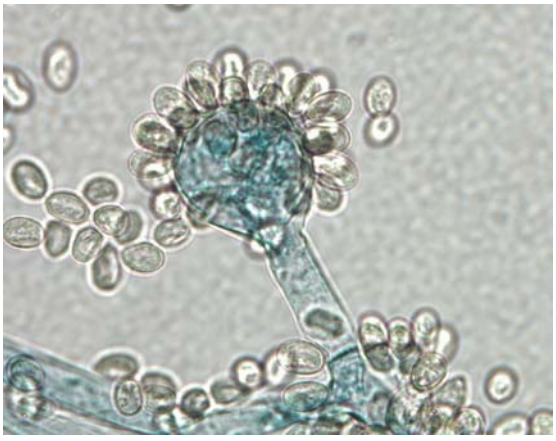


Last Issue's Picture Quiz Answer:



The photo is the mould *Aspergillus clavatus*. The isolate was received as a referred culture from a right bronchial washing. The colony was green and velvety. Microscopically, *A. clavatus* produces a distinctive club shaped vesicle with uniserate phialides. *A. clavatus* has been found to cause allergic aspergillosis and has been implicated in various pulmonary infections.

This Issue's Picture Quiz: What Mould is this?



This mould grew from a biopsy of a spreading subcutaneous infection in the leg of an individual with diabetes. On solid media, the colony grew rapidly and was grey and wooly with a pale yellow reverse. Microscopically, one celled spores formed on denticles on the surface of the vesicle.

Quality Control and Monitoring in Blood Gas Analysis

Teresa Miller, RRT, RPFT
Molecular Biology Section
(Excerpt taken from Original Publication)

Arterial blood gas (ABG) laboratory quality issues have been a topic of discussion for many years. Many different agencies concerned with laboratory quality have formulated different standards and definitions of what "quality" is in laboratory testing. The Quality System Essentials (QSEs) approach, as determined by NCCLS (formerly known as the National Committee for Clinical Laboratory Standards) and initially proven in the blood bank arena as a quality program, is a very comprehensive and practical guideline encompassing all quality issues in the AGB laboratory. The supportive documents have been recently updated as GP26-A2, "Application of a Quality System Model to Laboratory Services, Approved Guideline-Second Edition": and HS1-A "A Quality System Model for Health Care: Approved Guideline."

QSEs can be incorporated into any total quality management program and is a unique way to ensure quality from each analytical test. As any other test, ABG measurements are exposed to the three analytical areas that generally define quality issues: pre-analytical, analytical and post-analytical. Pre-analytical errors produce the majority of quality issues for this type of analysis.

QSEs suggest development in 12 areas of infrastructure that will address most of the concerns of any ABG laboratory. The 12 essential ingredients in a quality system model consist of:

- Organization
- Personnel
- Equipment
- Purchasing and inventory
- Process control
- Documents and record
- Occurrence management
- Internal assessment
- Process improvement
- Information management
- Safety and facilities
- Service and satisfaction

For the entire article, including references and suggested reading, please refer to the AARC Times, December 2002, pgs 28-31.

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Where is My Quirkey Bug??

Sandip Shah
Reference Bacteriology Unit

Often the laboratory hears the question “Where is the identification for my quirky bug?.” Reference bacteriology receives about 2,000 unusual or dangerous clinical pathogens for identification and characterization each year. These isolates are far from routine and usually come to MDCH because commercial identification systems either cannot identify or fail to identify the isolates with any degree of confidence. The main reason for a longer turnaround time from MDCH when compared with the typical clinical laboratory is the reference nature of the work. Initially, the viability and purity of referred isolates is confirmed. Then traditional biochemical testing and frequently special testing, such as chromatographic analysis of whole cell fatty acids, are performed to characterize an isolate. Some biochemical tests are incubated for 14 to 21 days before a result can be generated. Additional tests or repeat testing could double that time. Fastidious isolates that are biochemically inert or are received mixed with other organisms may also influence turnaround time. Some clinical cultures such as a nasopharyngeal swab for the isolation of *Bordetella pertussis* are incubated and read for 14 days before being reported as negative. On rare occasions, high priority events like testing for the agents of bioterrorism or special epidemiological surveillance projects may delay the routine work.

Approximately 97 percent of the isolates received are identified in the MDCH laboratory. Some are forwarded to CDC for further studies or special testing. A history form completed by the submitting institution must accompany isolates submitted to CDC. Since CDC receives isolates from around the world, participates in epidemiological investigations and responds to all public health emergencies, the priority given an individual culture may be based upon medical and public health significance, staff availability and resources. Some unusual isolates cannot be identified and are placed in a culture collection. It may take several years before an identification is available for these organisms. The Data and Specimen Handling (DASH) unit tracks all specimens submitted to CDC to ensure that results are reported as quickly as possible.

This should shed some light on the *modus operandi* for isolates submitted to reference bacteriology. Submitting agencies are encouraged to contact MDCH when questions arise about specimen submission or about progress on a particular isolate. It is strongly suggested that submitting laboratories save, preferably by freezing, all isolates sent to MDCH for identification. This eliminates problems caused by samples lost or broken in transit and those not viable on receipt. Please notify MDCH of problems related to mailed or faxed reports as soon as possible, so that delays in reporting can be avoided. It is suggested that this issue of *LabLink* is circulated to all laboratory staff in your facility. As always, your suggestions to improve our service are welcome. If you plan to be in the Lansing area, we invite you to visit our facility to see what we do and how we do it.

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